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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/889,203 | 03/13/2002 | Tracey Brown | 63370(49917) | 8511 |

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| EXAMINER | |
|---|---|
| FUBARA, BLESSING M | |
| **ART UNIT** | **PAPER NUMBER** |
| 1618 | |

DATE MAILED: 03/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/889,203 | BROWN, TRACEY | |
| | Examiner | Art Unit | |
| | Blessing M. Fubara | 1618 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *28 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

Examiner acknowledges receipt of power of attorney filed 11/02/05, request for extension of time, declaration under 37 CFR 1.132, amendment and remarks filed 10/28/05. Claims 1-9 are pending.

### NEW MATTER

### *Claim Rejections - 35 USC § 112*

1. Claims 1-9 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The recitation of hyaluronic acid having molecular weight of greater than or equal to 750,000 Daltons is new matter. Although applicants in the amendment that inserted the molecular indicated that there is support for the amendment in the specification as originally filed, the specific page and lines in the specification providing the support was not stated and Examiner does not find support for the amendment.

Applicant's specification at page 39, line 31 has 700,000 kDa; page 40, line 16 has 700 kDa; page 29, line 28 has 890,000 kDa and page 17, line 37 has 890,000 kDa; the lower molecular weight range is thus not 750 kD. Thus a molecular weight of equal to 750 kD is new matter and has no support in the specification as originally filed.

### *Claim Rejections - 35 USC § 102*

2. The rejection of claims 1, 6, 7 and 9 under 35 U.S.C. 102(e) as being anticipated by Turley et al. (US 6,475,795 B1) is withdrawn in view of the amendment specifying that the cytotoxic agent is non-nucleic acid.

***Claim Rejections - 35 USC § 103***

3. Claims 1-9 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Falk et al. (US 5,985,850).

Applicant argues that Falk does not co-administer high molecular weight hyaluronic acid and declares under 37 CFR 1.132 that hyaluronic acid of 30 kD was not as effective as hyaluronic acid having molecular weight of 824 kD.

4. Applicant's arguments and the declaration filed 10/28/05 have been fully considered but they are not persuasive.

The declaration is not commensurate with the claims. The claimed hyaluronic acid has a molecular weight of equal to or greater than 750 kD. However, no data is provided at a molecular weight of 750 kD or 700 kD. The 30 kD is much lower that the claimed 750 kD. The rejection follows below.

Falk discloses injectable formulations comprising anti-cancer agent or chemotherapeutic agent and hyaluronic acid (column 10, lines 8-59). The preferred molecular weight for the hyaluronan is less than 750,000 Daltons (claims 142, 83, 84 and 92). Applicant's declaration is not commensurate with 750 kD. Thus, the demonstration provided in applicant's declaration has no data at the lower end of 750 kD and the 30 kD data is much lower than 750 kD.

Therefore, there is no conclusive factual evidence that molecular weight equal to 750,000 Dalton provides unusual and unexpected results. Therefore, the evidence provided does not support hyaluronic acid having molecular weight of equal to 750,000 Daltons as being inventive over the disclosure in the prior art of a molecular weight of less than 750,000. Therefore, it would have been obvious to on of ordinary skill in the art at the time the invention was made to inject a composition comprising hyaluronic acid and anti-cancer agent to a subject in need thereof. One having ordinary skill in the art would have been motivated to use hyaluronic acid having the appropriate molecular weight that would provide the desired therapeutic effect and viscosity of the composition.

5. Claims 1-9 remain rejected under in the alternative, under 35 U.S.C. 103(a) as obvious over Turley et al. (US 6,475,795 B1) in view of Sola et al. (US 6,214,860).

Turley discloses pharmaceutical composition that comprises anti-sense nucleic acid bound to hyaluronic acid for treating diseases or conditions treatable using gene therapy (column 6, line 60 to column 7 line 10; column 2, line 62 to column 3 line 7 and claims 1-8). Turley specifically discloses that hyaluronan having a molecular weight of between 150,000 Daltons and 750,000 Daltons is preferred (column 7, lines 11-15 and 33; column 9, lines 37-40; claims 2 and 3). In column 7, line 64, hyaluronan having molecular weight of between 500,000 and 800,000 is used and larger molecular weight hyaluronan can be used in Turley except for hyaluronan having molecular weight exceeding 1,000,000 because at greater that 1,000,000, the hyaluronan self aggregates (column 10, lines 7-14). On the basis that Turley discloses larger molecular weight hyaluronan up to 1,000,000 but not exceeding, 1,000,000, there is then a disclosure for use of hyaluronan having molecular weight of greater than 750,000 in the

formulation of Turley. There is a disclosure for composition comprising hyaluronic acid having molecular weight of 500,000 to 800,000 Daltons and a composition that may have hyaluronan having preferred molecular weight of between 15,000 and 750,000 Daltons. Since molecular weight of 800,000 Daltons is greater than 750,000 Daltons, Turley renders obvious a molecular weight of greater than 750,000 Daltons is not inventive over the prior art. The declaration submitted by applicant is not commensurate with the claims.

Turley discloses anti-sense nucleic acid as the cytotoxic agent. Turley does not disclose non-polynucleic acid based cytotoxic agent. But one cytotoxic agent can be used in place of another with the expectation of producing antineoplastic effect. Sola recognizes paclitaxel, cisplatin and camptothecin as cytotoxic agents. Therefore, it would have been obvious to on of ordinary skill in the art at the time the invention was made to inject a composition comprising hyaluronic acid and anti-sense agent to a subject in need thereof. One having ordinary skill in the art would have been motivated to use other cytotoxic agents such as paclitaxel, cisplatin and camptothecin as cytotoxic agents in place of the anti-sense nucleic acid with the expectation that these substitutes will provide antineoplastic effect.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 3:30 p.m. (Monday to Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 7571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BF

Blessing Fubara
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VICKIE KIM
PRIMARY EXAMINER